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CASWELL
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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AD HOC MEETING 11/21/89
NOV 29, 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Trifluralin Mouse Cancer Study

FROM: William L. Burnam, Deputy Director
Health Effects Division (H7509C)

TO: Penelope Fenner-Crisp
Reto Engler
Karl Baetcke
Marcia Van Gemert
Hugh Pettigrew
Bruce Jaeger

The consensus of the attendees was that incidence of male liver tumors found in the Hoechst trifluralin study was insufficient to cause trifluralin to be returned to the HED Peer Review Group.

cc: Rick Tinsworth
Caswell File 889

Attachment

Trifluralin Mouse Study

Issue: The initial review of Hoechst trifluralin mouse cancer study indicated a possible compound-related effect on liver tumors in males. Historical control data were requested. The problem of liver tumors in male mice needs to be addressed quickly since trifluralin may be the test pesticide in the Agency's response to NRDC's 409 tolerance petition.

Background: The attached peer review indicates that trifluralin was a C carcinogen based on positive effects in male and female rats. In males, it produced an increase in follicular cell adenomas and carcinomas in thyroid and malignant neoplasms of the renal pelvis; in females it caused an increased incidence of benign urinary bladder tumors. A Q_1 of 7.7×10^{-3} is currently used for risk assessments based on the combined incidence of the above mentioned tumors. Trifluralin was not oncogenic in the B6C3F1 mouse at doses up to 4500 ppm.

Discussion: The male mouse liver data are as follows:

	Dose (ppm)			
	0	50	200	800
No. examined	50	50	50	50
Hepat. adenoma	5 (10)	8 (16)	7 (14)	6 (12)
Hepat. carcinoma	1 (2)	3 (6)	7 (14)	4 (8)
Combined	6 (12)	11 (22)	14 (28)	10 (20)

percents in (___)

According to Hugh Pettigrew, a pair-wise comparison of total liver tumors between the control and mid dose gives a value of $P=0.039$. The Peto trend analysis (attached) indicates that there is no significant trend for either the adenomas, carcinomas or combined adenomas and carcinomas.

The historical control information (attached) indicates that for similar studies of 2 year duration the average values for adenomas in males was about 10% (using the top 7 studies). The average value for carcinomas was about 3.4% for the same 7 studies. The controls in this study are very similar to past values while all treated groups are elevated. There is evidence from two of the studies that combined liver tumor values of 20% have occurred while another study showed a low of 4% combined incidence.